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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/933,638	08/20/2001	Aleksey G. Kazantsev	01997-289001	6696

26161 7590 09/22/2004

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EXAMINER	
DESAI, ANAND U	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/933,638	KAZANTSEV ET AL.	
	Examiner	Art Unit	
	Anand U Desai, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, and 18-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 18-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to amendment filed on June 1, 2004. Claims 2-17 have been cancelled. Claims 18-44 have been added. Claims 1, and 18-44 are currently pending and are under examination.

Priority

2. The oath filed on May 2, 2002 claims foreign priority to PCT/US01/26097 filed August 20, 2001. The PCT designates the U.S., therefore the current application should claim priority under Title 35, United States Code § 120. A specific reference to PCT/US01/26097 is missing from the first sentence of the specification.

Withdrawal of Objections and Rejections

3. The objection to underlined text within certain headings and the volume numbers in referenced journal articles is withdrawn.

1. The rejection of claims 1-11 under 35 U.S.C. 103(a) as being unpatentable over Housman et al. (U.S. Patent 6,420,122) in view of Preisinger et al. (Phil. Trans. R. Soc. Lond. B (1999) 354:1029-1034) is withdrawn.

Maintenance of Objections and Rejections

Specification

4. The disclosure is objected to because of the following informalities:

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Suggest, "Inhibition of protein-protein interaction of poly-glutamine containing polypeptides".

6. The abbreviation "HEAT" is not defined on page 7, line 8.

7. There is a typographical error on page 23, lines 1, and 14. The designation "HeLa" has an extra e in front; "eHeLa" appears to be intended to be "HeLa".

8. On page 23, line 7, the word for the restriction enzyme, *BamHI* is not italicized as is standard in the art.

9. On page 23, lines 13, 14, and 22, the abbreviation for "COS-1" and "COS-7" cells should be capitalized.

10. On page 27, lines 22 and 23, the sentence is incomplete. What happens to early adult?

11. The use of the trademark "TRANSFECTAM" has been noted in this application on page 23. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Appropriate correction is required.

Claim Objections

1. Claims 23, 30-32, and 36 are objected to because of the following informalities:

2. In claims 23, 30-32, and 36 the proper nouns, Huntingtin, and TATA, are not capitalized.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 37 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. In claim 37, it is not clear what proteins are encompassed by an amyloid-associated protein designation? If applicant submitted either a representative set of proteins known in the art and/or disclose specific amino acid sequences the phrase amyloid-associated protein would become clearer.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 18, 19, 20, 28, 29, 30-35, and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Peterson, et al. (Science 248:1625-1630 1990). Peterson et al. teach the cloning of human TATA binding factor comprising SEQ ID NO:11 (see pp. 1626, figure 1B, amino acids 270-337, current application, claims 1,28, 30, and 33) and SEQ ID NO:12 (see pp. 1626, figure 1B, current application, claims 1, 28, 30, 31-35). TATA binding protein contains multiple protein binding domains that binds coactivator transcription factors that contain multiple consecutive glutamine residues (see pp. 1625-1626, 3rd and 4th paragraphs, current application, claim 38). Once the coactivator transcription factors are bound to the TATA binding protein

they are physically separated, and coactivator transcription factors do not bind to each other. TATA binding protein comprises alpha-helical and beta-sheet structural motifs (current application claims 1, 18, 19, 20, and 28-35).

Response to Applicant's Remarks

Applicant's remarks state that amended claim 1 is directed to a therapeutic agent that prevents interaction between a first protein and a second protein, and that TATA binding protein (TFIID) disclosed by Peterson cannot meet this limitation. Applicant's state that TFIID facilitates the interaction of the general transcription factors, TFIIA or TFIIB in a way that promotes gene expression, thus TFIID does not, prevent the interaction of proteins. Therefore, Peterson et al. does not anticipate the therapeutic agent now claimed. This is not found persuasive. The phrase, "prevents interaction" is being interpreted with a broad reasonable interpretation that can encompass, describing the action of keeping the first protein physically away from the second protein and thus preventing a protein-protein interaction. Applicants own dependent claims 40 and 43 interpret the word, "interaction" as aggregation, and dimerization, thereby describing and suggesting multiple types of interactions. Therefore, the TATA binding protein disclosed in Peterson et al. does anticipate the claims as described in the 35 U.S.C. 102(b) rejection (see 102(b) rejection).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 18-22, 24-28, 34-36, and 38-44 rejected under 35 U.S.C. 103(a) as being unpatentable over Burke et al. (U.S. Patent 6,632,616 B2) in view of Huston et al. (U.S. Patent 5,525,491).

Burke et al. discloses polypeptide compounds that selectively bind to expanded polyglutamine repeats (see U.S. Patent '616, column 2, lines 15-25). The peptides can be used to slow or prevent disease pathology (see U.S. Patent '616, column 2, lines 7-10). The peptide compound is represented by the formula X^1-R^{11}-R^{12}-R^{13}-R^{14}-Y^1,

wherein:
R^{11} is Trp;
R^{12} is (i) Trp or (ii) a charged amino acid such as Lys, Arg or His (preferably Lys or Arg, and most preferably Lys);
R^{13} is (i) Trp or (ii) a charged amino acid such as Lys, Arg or His (preferably Lys or Arg, and most preferably Lys);
subject to the proviso that one of R^{12} and R^{13} is Trp and the other is a charged amino acid;
R^{14} is Trp;
X^1 is a polypeptide consisting of from zero to 5, 10 or 20 or 30 amino acids, preferably standard amino acids; and
Y^1 is a polypeptide consisting of from zero to 5, 10 or 20 or 30 amino acids, preferably standard amino acids;
or a physiologically or pharmaceutically acceptable salt thereof. Compositions comprising compounds as described above in a pharmaceutically acceptable carrier, and the use of such compounds for the preparation of a medicament for the treatment of disorders as described herein, are also aspects of the present invention. (see U.S. Patent '616, column 2, lines 26-48). The compounds may be conjugated to a heterologous protein or peptide, such as a translocation peptide, in accordance with known techniques (see U.S. Patent '616, column 3, lines 7-9). Burke et al. does not disclose a third domain that separates the first domain from the second domain.

Huston et al. discloses serine-rich peptide linkers that are used to design fusion proteins, which are 1.) soluble at high concentrations in physiological media, and 2.) resistant to proteolytic degradation (see U.S. Patent '491, column 1, lines 9-10, and 52-55). The peptide linker can be used to fuse one biologically active polypeptide to another biologically active peptide thereby forming a bi-functional fusion protein expressing both biological activities (see U.S. Patent '491, column 2, lines 38-41, and claims 1, and 2).

One would have been motivated to produce a therapeutic agent comprising the polypeptide compounds that selectively bind to expanded polyglutamine repeats to slow or prevent disease pathology, and one would have been motivated to use a linker domain disclosed by Huston et al. to multimerize the compound disclosed by Burke et al., since Burke et al. also suggests a dimeric analog of the compound, and a compound conjugated to heterologous protein or peptide (see U.S. Patent '616, column 10, lines 36-64). Furthermore, one would have expected the dimerized polyglutamine binding protein to retain biologically activity, since Burke et al. have shown a reduction in aggregation upon the administration of a dimerized compound (see U.S. Patent '616, Figures 4, and 5, the $(QBPI)_2$ compound, Table 1, column 21, and column 24, lines 24-28). Therefore, it would have been obvious to a person having ordinary skill in the art to synthesis a therapeutic agent that selectively binds polyglutamine containing peptides to slow or prevent disease pathology (current application, claims 1, 18-22, 24-28, 34-36, and 38-44).

8. Claims 1, 18-28, 34-36, and 38-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burke et al. (U.S. Patent 6,632,616 B2) in view of Huston et al. (U.S. Patent 5,525,491) as applied to claims 1, 18-22, 24-28, 34-36, and 38-44 above, and further in view of Housman et al. (U.S. Patent 6,420,122 B1). Housman et al. discloses a polypeptide with extended polyglutamine regions. The polypeptide contains the first 17 amino acids of the Huntingtin protein fused to 25 glutamine residues and fused with either a 28 amino acid c-myc tag or a 230 amino acid enhanced fluorescent protein tag (see U.S. Patent '122, column 12, lines 64 through column 13, line 10).

One would have been motivated to produce a therapeutic agent comprising the polypeptide compounds that selectively bind to expanded polyglutamine repeats to slow or prevent disease pathology, and one would have been motivated to use a linker domain disclosed by Huston et al. to multimerize the compound disclosed by Housman et al., since Housman et al. also suggests a compound conjugated to heterologous protein or peptide (see U.S. Patent '122, column 2, lines 42-44, and 49-64). Furthermore, one would have expected the dimerized polyglutamine binding protein to retain biologically activity, since Housman et al. have shown maintenance of biological activity of the heterologous compound (polyglutamine interaction of recombinant protein fused to a label) (see U.S. Patent '122, Examples 3-6). Therefore, it would have been obvious to a person having ordinary skill in the art to synthesis a therapeutic agent that selectively binds polyglutamine containing peptides to slow or prevent disease pathology (current application, claims 1, 18-22, 24-28, 34-36, and 38-44).

Response to Applicant's Remarks Regarding 35 U.S.C. § 103

Applicants traverse the 35 U.S.C. § 103. The traversal is based on the assumption that the three criteria for a *prima facie* case of obviousness are not met. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the

prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants state on the 3rd paragraph of the 35 U.S.C. § 103 section of the remarks, the present 35 U.S.C. § 103 rejection has "no suggestion whatsoever that one should make a therapeutic agent having three domains, the third of which separates a first domain from a second domain to such an extent that proteins bound to the first and second domains cannot interact as they otherwise would." Applicants state Housman and Preisinger do not teach therapeutic agents having the first, second, and third domains required by Applicant's claim 1 (and by the claims that depend therefrom), nor is there motivation in those disclosures to modify the polyglutamine containing proteins Housman and Preisinger used to arrive at the therapeutic agents Applicants now claim. Applicants see nothing in Housman's and Preisinger's disclosure that would provide one of ordinary skill in the art with a reasonable expectation that the therapeutic agents now claimed would succeed.

However, Housman et al. does suggest polyglutamine containing polypeptides that are potentially useful as therapeutics for the treatment of disease conditions associated with protein aggregations mediated by abnormal protein-protein interactions mediated by elongated polyglutamines (see U.S. Patent '122, column 1, lines 45-51, column 5, lines 29-35, and column 9, lines 19-25). Housman et al. discloses the polyglutamine containing polypeptides as being either naturally or non-naturally occurring polypeptides that have at least 32 consecutive glutamine residues that will aggregate with other polyglutamine containing peptides (see U.S. Patent '122, column 2, lines 5-7, and 33-35). Housman et al. also discloses the ability to maintain biological activity of a heterologous polypeptide containing the first 17 amino acids of

Huntingtin with polyglutamine amino acid residues fused to a fluorescent label, therefore one would have expected a dimerized heterologous polypeptide to retain biological activity of sequestering polyglutamine containing peptides and thereby treat disease conditions.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 17, 2004

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER